8. A method of modulating the level of a nitrate-responsive root transcriptional factor in a plant, comprising:

(a) introducing into a plant cell a recombinant expression cassette comprising polynucleotide encoding a polypeptide having root transcriptional factor activity of claim 1 operably linked to a promoter;

(b) culturing the plant cell under plant cell growing conditions;

(c) regenerating a plant from said plant cell; and

(d) inducing expression of said polynucleotide for a time sufficient to modulate the level of nitrate-responsive root transcriptional factor in said plant.

9. The method of claim 8, wherein said plant is maize.

REMARKS

Reconsideration of the present application is respectfully requested. The Examiner is requested to enter the amendments submitted, as Applicants believe that these amendments put the claims in condition for allowance. Applicants respectfully reserve the right to file a divisional application or take other such appropriate measures to protect the subject matter in the cancelled claim.

Status of the Claims

Claims 1 - 9 remain in this application. Claim 10 has been cancelled without prejudice. Claims 1, 2, 4, 8 and 9 have been amended.

Support for the amended claims is found throughout the specification, most notably pages 21-22, 33-38, 44-46, and 53. No new matter has been added by way of amendment to the claims.

Attached hereto is a marked-up version of the changes made by the current amendment. The attached page is captioned **"Version with markings to show changes made".**

Claim Objections

The Examiner objected to claims 2, 4, and 8, because they contain minor informalities.

In an effort to expedite prosecution and to better define the claimed invention, Applicant has amended claims 2, 4 and 8 to include the Examiner's suggested language.

Rejections under USC § 101

The Examiner has rejected claims 1-9 under 35 U.S.C. § 101, because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. The Examiner states that "given the low level of identity of SEQ ID NO: 1 with ANR1 and the 100% identity of instant SEQ ID NO: 2 with a pollen-expressed transcription factor, it does not appear that SEQ ID NO: 1 encodes a nitrate-responsive root transcription factor." Further the examiner asserts that "while expressing the claimed nucleotide sequences in plants is interesting from a basic science standpoint, since the specification does not teach the function or identity of SEQ ID NOS: 1 and 2, further basic research is required to determine if SEQ ID NO: 2 functions as a nitrate-responsive root transcription factor." Therefore the Examiner concludes that since the claims are seen as failing to meet the criterion of a substantial utility, it is concluded that the specification does not disclose any utility for the claimed isolated nucleic acids.

Claims 1, 2, 4, 8 and 9 have been made to better clarify the claimed subject matter and to respond to Examiner's suggestions.

Contrary to the Examiner's assertion, simply comparing the sequence identity of the ANR1 and pollen-expressed transcription factors to the disclosed sequences is not enough evidence to conclude that claimed SEQ ID NO: 1 is not a root transcriptional factor polynucleotide. SEQ ID NO: 1 has been determined by the applicant to be expressed primarily in roots based on the Lynx MPSS Expression Analysis Method (See Declaration of Dr. Wesley Bruce submitted herewith). The polynucleotide expression was found in lateral roots as well as whole roots. The expression pattern of this polynucleotide is represented in 58% of the applicant's proprietary maize root cDNA libraries. Whereas the polynucleotide was expressed in only 6% of the maize tassel cDNA libraries and was undetectable in any of the proprietary maize pollen cDNA libraries. These results support that the instant transcriptional factor polynucleotide is primarily expressed in root tissue, and therefore does not fit a pollen specific expression pattern. Based on the foregoing, the applicant disagrees with the statement that the cited pollen expressed transcription factor is the same as the root transcriptional factor of the instant invention. The expression distribution across applicant's proprietary maize libraries shows SEQ ID NO: 1 is predominantly expressed in maize roots, including the maize lateral root tissues, and minimally in tassel related tissues. This suggests that SEQ ID NO: 1 is transcription factor functioning in maize root systems.

Examiner has stated that the specification discusses "a signal transduction pathway that links external nitrate to increase lateral root proliferation and that manipulation of nitrate-responsive genes such as ANR1 in agronomic crops could be of value in maximizing plant utilization of available nitrogen and in reducing agricultural nitrogen inputs, that improved control of lateral root proliferation could have useful applications in soil remediation, that increased root biomass may be beneficial in production of specific structural carbohydrates, and that manipulation of nitrate-responsive genes could also be useful in stimulating root proliferation of cuttings for plant propagation". The applicant submits that the polynucleotide disclosed and claimed as SEQ ID NO: 1 functions as a nitrate- responsive transcription factor in maize root systems. Therefore Applicant believes that the present invention has a well-

established utility for which has been proposed a specific, substantial and credible use in the present application. Applicant respectfully requests that the rejection based on U.S.C. § 101 be withdrawn.

Rejections under 35 USC § 112 second paragraph

The Examiner has rejected claims 1-9 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Examiner states that the recitation of "member" in line 1 of claims 1 and 2, render the claims, and those dependent thereon, indefinite. Examiner also indicates that there is an improper antecedent basis in claim 2 for "a member of claim 1", and also an improper antecedent basis in claim 8 for "root transcriptional factor polynucleotide of claim 1".

Applicants have noted the Examiner's point regarding the ambiguity detected in the claims as originally submitted. Applicants would like to thank the Examiner for his suggestion regarding rephrasing. Claims 1, 2 and 8 have been amended to correct the language. Applicant requests that the rejections to claims 1-9 under U.S.C. § 112, second paragraph be withdrawn.

Rejections under U.S.C. 112 § first paragraph

The Examiner has rejected claims 1-9 under U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such as way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner asserts that there is no evidence provided that shows that all the structurally defined polynucleotides of the invention related to SEQ ID NO: 1 will encode a polypeptide having root transcriptional factor activity.

In an effort to expedite prosecution, claims 1, 2, 4, 8 and 9 have been amended to better describe and clarify the subject matter claimed as the invention. Applicant

submits that these polynucleotides as claimed are not limited simply by structure, but are in fact further limited by the explicit functional requirement that the encoded polypeptide must have root transcriptional factor activity. Given this explicit requirement of root transcriptional factor activity imposed on the sequences, there is no requirement for providing additional evidence of such functionality.

Applicant notes that there is no *per se* requirement for such evidence, and that in fact the appropriate test of adequate written description is that "a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention." Manual of Patent Examining Procedure, §2163 (quoting *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991)).

In the instant case it is clear that the skilled artisan would recognize the coherence and extent of the genus of nucleotide sequences of the invention that are constrained to encode polypeptides with root transcriptional factor activity, and that therefore the claims are supported by adequate written description.

The Examiner has rejected claims 1-9 under U.S.C. §112, first paragraph, stating "since the claimed invention is not supported by either a credible asserted utility or a well established utility...one skilled in the art would not know how to use the claimed invention." Further the Examiner suggests that sequences that "differ from SEQ ID NO: 1 by as much as 75%" may not share its functional activity. The Examiner states that undue experimentation would be required by one skilled in the art to produce polynucleotides that differ in sequence from SEQ ID NO: 1 but still retain its function.

Applicants respectfully submit that the sequences as originally claimed would be able to be reproduced by one of skill in the art. The specification is not required to disclose all possible permutations defined by claiming 75% identity to SEQ ID NO: 1. The specification is required to provide sufficient disclosure and enablement so that one skilled in the art could make the embodiments encompassed by the claims.

> The function of [the] description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him; to comply with the description requirement, it is not necessary that the application describe the claimed invention in *ipsis verbis*; all that is required is that it reasonably convey to persons skilled in the art that, as of the filing date thereof, the inventor had possession of the subject matter later claimed by him. *In re Edwards* 568 F. 2d at 1351-52, 196 U.S.P.Q. at 467

Claims 1, 2, 4, 8 and 9 have been amended for clarity, and now include 97.5% GAP sequence identity percentage limitations across the full length of SEQ ID NO:1, as found in the specification, page 25. The present application provides sufficient information and guidance to enable one of skill in the art to make and use a polynucleotide with 97.5% sequence identity as determined by the GAP algorithm under default parameters, across the full length of the claimed sequence. The specification provides a working example of the isolation of DNA sequencing and identification on pages 63-64.

The specification describes variants and identification of sequences resulting from site-directed mutagenesis (pages 7 and 19) that would encompass sequences with at least about 97.5% sequence identity to SEQ ID NO:1. The specification provides information suitable for isolating the sequences, their variants and the mutations, and methods for identifying the variants and mutations. Methods for inducing mutations and variants are well known to those of skill in the art such as the use of degenerate PCR cycles (Gould et al. Proc Natl. Acad. Sci. USA, 86:1934-1938 (1989)) and oligonucleotide mutagenesis (F.M. Ausubel et al., Eds., Current Protocols, a joint venture between Greene Publishing Associates, Inc. and John Wiley & Sons, Inc. (1995)).

The Examiner asserts there is no way to predict which polynucleotides would be functional, and therefore further asserts that the construction and screening involved would cause undue experimentation. The Applicant respectfully traverses the assertion.

> It is well established that only "when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required" *Genentech, Inc. v. NovoNordisk, 108 F3d 1361, 42 USPQ2d 1001 (Fed. Cir. 1997).*

The specification provides ample disclosure of starting material such as appropriate tissues (see Example 1, pages 55-56 of the specification) and construction process (pages 29-33). By using the disclosed materials, examples, and the established protocols cited in the specification, one of skill in the art would readily be able to synthesize any number of sequences as claimed in amended Claim 1.

The Examiner concludes that "given the breadth of the claims, unpredictability of the art and lack of guidance of the specification...undue experimentation would be required by one skilled in the art to make and use the claimed invention."

> Enablement is lacking in cases where the undescribed embodiments cannot be made, based on the disclosure in the specification, without undue experimentation. The question of experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is the amount of experimentation must not be unduly extensive. *PPG Inc. V. Guardian Industries Corp.* (37 USPQ 1218, 1623, (Fed. Cir. 1996))

The present specification provides reasonable guidance with respect to the direction in which the experimentation should proceed by providing sequences, methods, citations and examples sufficient to practice the scope of the claims. While the methods require selection of polynucleotide exhibiting the desired activity, the selection is routine and would not require undue experimentation. No matter how much detail is provided, one will have to select for the desired function.

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction

in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. *Ex parte Jackson*, 217 USPQ 804, 807 (1982 PTOBA).

In an effort to expedite prosecution, claims 1, 2, 4, 8 and 9 have been amended to cancel without prejudice reference to the polypeptide disclosed as SEQ ID NO: 2 and all variants which have less than 97.5% sequence identity to SEQ ID NO: 1. In addition, Claims 1, 2, 4, 8 and 9 have been amended in an effort to expedite prosecution and to better define the claimed invention.

With the guidance provided in the present specification, one skilled in the art can readily practice the claimed invention.

As Applicant has responded to the utility rejection under 35 U.S.C. § 101, it is believed that the utility rejection has been overcome. Applicant respectfully submits that the claims as amended are now in a proper condition for allowance and request the rejections to claims 1 – 9 under 35 U.S.C. § 112 be withdrawn.

Rejections under U.S.C. § 102

Examiner has rejected claims 1-3 under 35 U.S.C. §102(a) as being anticipated by *Heuer et al.* (Sex. Plant Reprod., Vol. 13, pages 21-27). Examiner states that the reference teaches a polynucleotide with 86.7% sequence identity to SEQ ID NO: 1, and comprises at least 50 contiguous nucleotides of instant SEQ ID NO: 1. Also, the reference teaches a polypeptide with 100% sequence identity to SEQ ID NO: 2. The Examiner therefore asserts that the reference describes the invention of the instant application.

Applicant respectfully disagrees. In an effort to further prosecution, and to better describe the claimed invention, claims 1 and 2 have been amended. Newly revised claims 1 and 2 as so amended, do not read on the subject matter of the *Heuer et al.* reference, and do not relate to the pollen specific activity of that reference. Applicant respectfully requests that the rejection of claims 1-3 based on 35 U.S.C. § 102(a) be withdrawn.

Examiner has rejected claims 1-4, 7 and 8 under 35 U.S.C. §102 (b) as being anticipated by *Zhang et al.* (Science, 1998, Vol. 279, pages 407-409). Examiner notes that the reference teaches an ANR1 sequence which would have the property of being "amplified from a nucleic acid library using primers which selectively hybridize under stringent conditions to loci within a polynucleotide of SEQ ID NO: 1".

The *Zhang et al.* reference cited does not anticipate the invention of the current application.

> To constitute an anticipation, a reference must disclose within its four corners each and every element of the claimed invention. *Structural Rubber Products Co. v. Park Rubber Co.*, 749 F. 2d 707, 223 U.S.P.Q. 1264 (Fed. Cir. 1984); *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 U.S.P.Q. 773 (Fed. Cir. 1985); *Hybritech Inc. v. Monoclonal Antibodies Inc.*, 802 F.2d 1376, 231 U.S.P.Q. 81 (Fed. Cir. 1986).

The sequences of the reference do not fall within the claim limitations, and do not enable someone to practice the invention. Further the Federal Circuit has held:

> "a reference must enable someone to practice the invention in order to anticipate under § 102(b)" *In Symbol Technologies, Inc. v. Opticon, Inc.*, 935 F.2d 1569, 19 USPQ2d 1241 (Fed. Cir. 1991).

The sequence claimed in the current application is a sequence having at least 97.5% sequence identity, as determined by the GAP algorithm, using default parameters, across the full length of SEQ ID NO: 1. The sequence of *Zhang et al.* would not be at least 97.5% homologous to the entire claimed sequence of the present invention.

Applicant submits that the reference cited by the Examiner does not teach the features of the presently claimed invention and thus does not anticipate. It is respectfully requested that the rejection of claims1-4, 7 and 8 under 35 U.S.C. § 102(b) be withdrawn.

Rejections under U.S.C. § 103

Examiner has rejected claims 1-9 under U.S.C. 103(a), as being unpatentable over *Zhang et al.* in combination with *Fromm et al.* (Biotechnology, 1990, Vol. 8, pages 833-839) the Examiner states that *Zhang et al.* teaches transgenic Arabidopsis plants transformed with the ANR1 cDNA in sense or antisense orientation. *Zhang et al.* do not teach transgenic maize plants. *Fromm et al* teach a method for producing transgenic maize plants. The Examiner asserts that it would have been obvious and within the scope of ordinary skill in the art at the time the invention was made to overexpress the ANR1 cDNA of *Zhang et al.* in any plant, including maize for various reasons.

Applicant has amended claims 1, 2, 4, 8 and 9. Current claims 1 - 9 distinguish over the combination of *Zhang et al.* and *Fromm et al.* by requiring a sequence not disclosed in either reference. Such a combination is not disclosed or suggested in the art. Absent the required sequence, the combination of the items cited by the Examiner does not teach or suggest the present invention. It should be noted that it is clear that in order to establish a background for finding obviousness under U.S.C §103, that the determination of the scope and contents of the prior art cannot be performed by the mere gathering of elements from separate and distinct disclosures irrespective of the teachings of the disclosures. There must be a reason apparent at the time the invention was made to select the particular combination or the references or the use of such teachings as evidence of obviousness with entail prohibited hindsight. In *re Nomiya*,184 U.S.P.Q. 607 (CCPA 1975).

Applicant submits that the currently amended claims were not obvious at the time the invention was made especially in light of the requirement of novel SEQ ID NO: 1. Applicant respectfully requests that the rejection of claims 1-9 under U.S.C. § 103(a) be withdrawn.

CONCLUSION

On the basis of the amendments and remarks, reconsideration of the application and its allowance are respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

1. (Amended) An isolated nucleic acid which encodes a polypeptide having root transcriptional factor activity comprising a [member] polynucleotide selected from the group consisting of:

(a) a polynucleotide having at least [75] 97.5% sequence identity, as determined by the GAP algorithm under default parameters,[to] across the full length of a polynucleotide of SEQ ID NO: 1;

[(b) a polynucleotide encoding a polypeptide of SEQ ID NO: 2;]

[(c) a polynucleotide amplified from a nucleic acid library using primers which selectively hybridize, under stringent hybridization conditions, to loci within a polynucleotide of SEQ ID NO: 1;]

[(d) a polynucleotide which selectively hybridizes, under stringent hybridization conditions and a wash in 0.1X SSC at about 60 to 65°C, to a polynucleotide of SEQ ID NO: 1;]

[(e)] (b) a polynucleotide of SEQ ID NO: 1; and

[(f)] (c) a polynucleotide which is complementary to a polynucleotide of [(a), (b), (c), or (e); and] (a) or (b).

[(g) a polynucleotide comprising at least 50 contiguous nucleotides from a polynucleotide of (a), (b), (c), (d), (e), or (f).]

2. (Amended) A recombinant expression cassette, comprising [a member] the nucleic acid of claim 1 operably linked, in sense or anti-sense orientation, to a promoter.

3. A host cell comprising the recombinant expression cassette of claim 2.

4. A transgenic plant comprising [a] the recombinant expression cassette of claim 2.

5. The transgenic plant of claim 4, wherein said plant is a monocot.

6. The transgenic plant of claim 4, wherein said plant is selected from the group consisting of: maize, soybean, sunflower, sorghum, canola, wheat, alfalfa, cotton, rice, barley, and millet.

7. A transgenic seed from the transgenic plant of claim 4.

8. A method of modulating the level of a nitrate-responsive root transcriptional factor in a plant, comprising:

(b) introducing into a plant cell a recombinant expression cassette comprising a [root transcriptional factor] polynucleotide encoding a polypeptide having root transcriptional factor activity of claim 1 operably linked to a promoter;

(c) culturing the plant cell under plant cell growing conditions;

(d) regenerating a plant from said plant cell; and

(e) inducing expression of said polynucleotide for a time sufficient to modulate the level of nitrate-responsive root transcriptional factor in said plant.

9. The method of claim 8, wherein [the] said plant is maize.

[10. An isolated protein comprising a member selected from the group consisting of:

(a) a polypeptide of at least 20 contiguous amino acids from a polypeptide of SEQ ID NO: 2;

(b) a polypeptide of SEQ ID NO: 2;

(c) a polypeptide having at least 75% sequence identity to, and having at least one epitope in common with, a polypeptide of SEQ ID NO: 2, wherein said

sequence identity is determined by the GAP algorithm under default parameters; and,

(d) at least one polypeptide encoded by a member of claim 1.]